Attorney Docket No. P29315 Application No. 10/569,556

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| Applicants | : Makoto OGISO | Group Art Unit : 3774 |
| Serial No | : 10/569,556 (National Stage of PCT/JP2003/10826) | Examiner: Joshua H. LEVINE |
| I.A. Filed | : August 27, 2003 | Confirmation No.: 7641 |
| For | : BIOCOMPATIBLE MATERIAL STRUCTURE IMPREGNATED WITH FINE BONE POWDER AND ITS PRODUCTION METHOD | |

**APPEAL BRIEF UNDER 37 C.F.R. § 41.37**

Commissioner for Patents
U.S. Patent and Trademark Office
Customer Service Window, Mail Stop Appeal Brief – Patents
Randolph Building
401 Dulany Street
Alexandria, VA 22314

Sir:

This Appeal Brief responds to the final Office Action mailed July 9, 2010 and to the Advisory Action mailed October 26, 2010, finally rejecting claims 1, 2, 5, 6, 9, 10, 14, 17-19, 22, and 25-28.

A Notice of Appeal in response to the Final Office Action was filed on November 3, 2010.

The requisite fee under 37 C.F.R. § 41.20(b)(2) for filing this Appeal Brief is being paid concurrently herewith. The Patent and Trademark Office is hereby authorized to charge any additional fees that may be deemed necessary for maintaining the pendency of this application, including any appeal or extension of time fees that may be deemed necessary, to Deposit Account No. 19-0089.

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## I. Real Party in Interest

The assignees, PENTAX CORPORATION and MAKOTO OGISO, are the real parties in interest, by virtue of an assignment recorded February 27, 2006 at Reel/Frame: 017710 / 0219.

## II. Related Appeals and Interferences

None.

## III. Status of Claims

Claims 1-6, 9-19, and 22-28 are pending. Claims 3, 4, 11-13, 15, 16, 23, and 24 are withdrawn. Claims 1, 2, 5, 6, 9, 10, 14, 17-19, 22, and 25-28 stand finally rejected.

Appellant appeals the rejection of claims 1, 2, 5, 6, 9, 10, 14, 17-19, 22, and 25-28.

## IV. Status of Amendments

The claims on appeal are in the form presented in the response filed April 16, 2010.

## V. Summary of Claimed Subject Matter

The following description is made with respect to the independent claims and includes reference to particular parts of the specification. As such, the following is merely exemplary and is not a surrender of other aspects of the present invention that are also enabled by the present specification and that are directed to equivalent structures or methods within the scope of the claims.

Independent claim 1 relates to a bone-powder-impregnated, porous structure comprising a porous matrix made of a biocompatible material impregnated with fine bone powder obtained by pulverizing living bones and/or teeth (specification, page 5, lines 5-8), wherein the fine bone powder comprises sub-micron particles (specification, page 13, line 28 – page 14, line 7).

Independent claim 17 relates to a bone-powder-impregnated, surface-roughened structure comprising a surface-roughened matrix made of a biocompatible material, which is impregnated with fine bone powder obtained by pulverizing living bones and/or teeth (specification, page 6, lines 3-6), wherein the fine bone powder comprises sub-micron particles (specification, page 13, line 28 – page 14, line 7).

## VI. Grounds of Rejection to be Reviewed on Appeal

A) Whether claims 1, 5, 6, 9, 10, 14, 17, 19, 22, and 25-28 are obvious under 35 U.S.C. § 103(a) over Smestad (U.S. Patent No. 4,430,760) in view of Trieu et al. (U.S. Patent Application Publication No. 2002/0115742).

B) Whether claims 2 and 18 are obvious under 35 U.S.C. § 103(a) over Smestad (U.S. Patent No. 4,430,760) in view of Trieu et al. (U.S. Patent Application Publication No. 2002/0115742) and further in view of Smith et al. (U.S. Patent Application Publication No. 2004/0253279).

## VII. Argument

### A. Whether claims 1, 5, 6, 9, 10, 14, 17, 19, 22, and 25-28 are obvious under 35 U.S.C. § 103(a) over Smestad (U.S. Patent No. 4,430,760) in view of Trieu et al. (U.S. Patent Application Publication No. 2002/0115742).

Prior to addressing the details of the rejection, Appellant provides some background for context. (The following is taken from the "BEST MODE FOR CARRYING OUT THE INVENTION" section of the specification, which begins on page 8, line 10.)

Repeated remodeling in healthy animal bone usually causes the coupling of absorption and regeneration in bone. However, the absorption and regeneration of bone are not always balanced.

In a bone fracture, a large amount of bone is formed in the injured portion, with slight bone absorption occurring. When a bone is bored, the formation of bone occurs so actively as to fill the hole, yet only slight bone absorption occurs in the cut surface of the bone. Also, when yellow bone marrow is washed away in the cancellous bone region, a large amount of bone is formed in that bone marrow region, yet bone absorption occurs only slightly on the original bone surface, which is the center of bone formation. These facts indicate that the bone inherently has the ability to regenerate more bone than it absorbs – i.e., it exhibits an excess self-regenerating function.

The bone matrix contains various proliferation factors, which contribute to the formation of bone. Bone morphogenetic protein, or "BMP," is a proliferating factor that is considered to function in an early stage of a bone-forming process, but it is difficult to form bone in humans simply by giving BMP alone. It is presumed that bone regeneration is occurring more than bone absorption when various bone-proliferating factors, including BMP, are freed from the bone and activated by bone absorption, acting on mesenchymal stem cells proliferated in an injured portion compositely, thereby efficiently providing a bone-regenerating environment around the point of bone absorption. The formation of bone in such environment starts when osteoblasts are

formed by differentiation on and near a bone surface on which bone absorption occurs. Thus, osteoblasts usually are not formed spontaneously in portions separate from the bone.

The mesenchymal stem cells that are differentiatable to osteoblasts do not always exist only in bone tissue. Undifferentiated mesenchymal cells or mesenchymal stem cells differentiatable to various cells, including osteoblasts, remain in soft tissues, such as connective tissues, muscles, etc., including fat tissues obtained from the mesenchymal tissue, which is an embryological origin of bone.

The absorption and regeneration of bone is balanced in the remodeling of healthy bone, such that no more bone than necessary is regenerated, and usually no bone is formed in fat tissues or muscles, presumably because of the lack of a bone morphogenetic protein (bone-forming factor) or the function of a bone morphogenesis-preventing factor.

Theses facts suggest that a large amount of bone can be formed not only in bone tissues, but also in fat tissues, fibrous connective tissues, and muscle tissues, if bone that contains the bone-forming factor is well used in an artificial space in which the bone morphogenesis-preventing factor can be excluded. In the course of bone formation, it is necessary to meet the conditions that the space becomes rich in the bone-proliferating factor freed from the bone, and that part of the bone remains.

Accordingly, the present invention provides a bone-powder-impregnated structure (porous or surface-roughened structure) comprising a biocompatible material capable of regenerating a large amount of bone from a small amount of bone, by setting an environment in which the maximum bone-regenerating function can be exhibited. In the present invention, the bone powder can be efficiently absorbed by osteoclasts and macrophages in the communicating macro-pores as quickly as possible after the implantation, to create an environment rich in the bone-proliferating factor necessary for bone formation in the porous structure, and to cause bone powder in the fine communicating pores or the recesses to avoid the attack of osteoclasts and macrophages, thereby inducing the differentiation of mesenchymal stem cells proliferated in the

communicating macro-pores to osteoblasts. Thus, a composite comprising a biocompatible material having fine communicating pores or recesses and fine bone powder received in the communicating pores or recesses acts as a scaffold for differentiation to osteoblasts. By causing these phenomena in the porous structure, the influence of a bone morphogenesis-preventing factor that is considered to exist in tissues outside the porous structure is excluded, making it possible to form a large amount of bone in the porous structure.

With this as context, the Office has rejected claims 1, 5, 6, 9, 10, 14, 17, 19, 22, and 25-28 as obvious under 35 U.S.C. § 103(a) over Smestad (U.S. Patent No. 4,430,760) in view of Trieu et al. (U.S. Patent Application Publication No. 2002/0115742).

Smestad discloses a bone prosthesis comprising particulate demineralized bone, dentin, or mixtures thereof, contained within a biocompatible, porous casing. The porous casing is, for example, a pouch or a container made from fabrics or microporous membranes. Smestad teaches that examples for fabrics are woven fabrics such as the Dacron/nylon/carbon composite fabrics, etc., or nonwoven fabrics made of collagen, polyesters, polyamides, or polyolefins, etc., and further, that the microporous membranes are made by forming pores in various kinds of dense polymers such as polycarbonates, polyamides, polyesters, polyolefins, polysaccharides, and cellulosics by well-known pore-forming techniques. Smestad mentions that demineralized bone is made by contacting bone with acid, such as hydrochloric acid, and that the particulate demineralized bone has a particle size in a range of about 40 to 500 μm, preferably 75 to 250 μm (column 2, lines 22-25).

The presently claimed invention differs from Smestad (at least) by Smestad's failure to disclose the use of living bone and the use of the presently claimed particle size of the bone powder. With respect to the presently claimed living bones and/or teeth, Appellant notes that living bone contains a large amount of apatite of regular arrangement, as well as proteins such as collagen, bone morphogenetic protein (BMP), etc. BMP supported on the regular-arranged apatite is a protein contributing to the formation of bone. Appellant notes that *demineralized* bone (which is what Smestad discloses) obtained by the treatment with acids, like hydrochloric

acid, comprises mainly protein such as collagen, but no longer contains apatite. Also, in the demineralized bone powder used in the bone prosthesis disclosed in Smestad, BMP supported on the regular-arranged apatite may be partly washed out together with the apatite by treatment with the acid. On the other hand, fine bone powder obtained by pulverizing living bones, as employed in the presently claimed invention, contains apatite together with collagen and BMP. Thus, bone powder of living bones can strongly support the bone-inducing capability and is capable of regenerating a large amount of bone (several tens of times) from a small amount of bone. Particularly, as also taught in the present specification, the use of autologous bones "is considered best to regenerate bone" with high capacity (see, e.g., specification, page 1, lines 13-15). Appellant respectfully submits that Smestad does not teach or suggests the use of living bones because it specifically teaches that bones should be demineralized. Accordingly, Appellant respectfully submits that Smestad fails to teach or suggest this feature of the claimed invention.

For the particle size, the Office relies on Trieu et al. The Office asserts that it would have been obvious to one of ordinary skill in the art to include the particles in Trieu et al. in a bone prosthesis in Smestad for the purpose of increasing the surface area of the particles to provide for advantageous biological and mechanical properties. Appellant respectfully disagrees.

Trieu et al. disclose an orthopedic composition comprising a homogeneous mixture of a biocompatible polymer and a bioactive particulate ceramic having an average particle size of not more than about 500 nm. The ceramic phase can be chosen from a wide variety of ceramics, including synthetic, natural, bioresorbable, or non-resorbable ceramics. For example, the ceramic phase may include bioactive glass and various calcium-containing ceramics, such as calcium phosphate-containing ceramics and including hydroxyapatite, α-tricalcium phosphate, β-tricalcium phosphate, and tetracalcium phosphate.

Appellant further respectfully submits that a person skilled in the art would not combine the Trieu et al. teaching with that of Smestad because the bioactive particulate ceramic has an average particle size of *not more than* about 500 nm in Trieu et al., whereas the demineralized

bone in Smestad must have a particle size in a range of about 40 to 500 μm, preferably 75 to 250 μm (column 2, lines 22-25). Smestad specifically states that the maximum pore size will be less than the minimum particle size of the demineralized bone or dentin powder; accordingly, for embodiments having particle sizes down to 40 μm, the maximum pore size will be below 40 μm (column 3, lines 23-28). Even if the casing lumen having a pore size of 5 μm, which is the *minimum* pore size in Smestad (column 3, lines 30-31), is used for the porous casing in which the bioactive particulate ceramic in Trieu et al. is contained, the bioactive particulate ceramic would leak out, because the ceramic has an average particle size of not more than about 500 nm. Thus, the bioactive particulate ceramic having an average particle size of not more than about 500 nm in Trieu et al. *could not be used* for the bone prosthesis in Smestad. Simply stated, the use of Trieu et al.'s particle size in Smestad's composition would render Smestad's composition unsatisfactory for its intended use.

The law clearly states that if a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). Appellant also notes that the law states that if the proposed modification of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959). Thus, Appellant submits that the Office's rejection is legally improper, on at least two legal bases, and respectfully requests its withdrawal for at least these reasons.

Finally, Appellant wishes to address comments made in the Advisory Action. The Advisory states that "Trieu et al. could use demineralized bone obtained from natural sources [presumably referring to Smestad]." Initially, Appellant notes that whether Trieu et al. *could* use demineralized bone obtained from natural sources [i.e., Smestad] presupposes that Trieu et al. *would* use demineralized bone obtained from natural sources. As explained above, a person skilled in the art would not combine the teachings of Smestad with those of Trieu et al. Perhaps

more importantly, even if Trieu et al. could and would use demineralized bone obtained from natural sources [i.e., combine Trieu et al. with Smestad], the present invention would not result, as it requires fine bone powder from pulverizing *living* bones and/or teeth.

In view of the foregoing, Appellant respectfully submits that a person skilled in the art would not have modified the bone prosthesis of Smestad or combined it with the bioactive particulate ceramic of Trieu et al. However, even if combined, the present invention would not result. For at least these reasons, Appellant maintains that independent claims 1 and 17 are novel and nonobvious over Smestad and Trieu et al., and that claims 2, 5, 6, 9, 10, 14, 18, 19, 22, and 25-28 are also patentable over Smestad and Trieu et al., at least because they depend from claims 1 or 17.

Appellant respectfully requests reversal of the rejection.

**B. Whether claims 2 and 18 are obvious under 35 U.S.C. § 103(a) over Smestad (U.S. Patent No. 4,430,760) in view of Trieu et al. (U.S. Patent Application Publication No. 2002/0115742) and further in view of Smith et al. (U.S. Patent Application Publication No. 2004/0253279).**

With respect to the Examiner's rejection of claims 2 and 18 as being unpatentable over Smestad in view of Trieu et al. and in further view of Smith et al. (U.S. Patent Application Publication No. 2004/0253279), although the Examiner asserts that Smith et al. teaches a porous structure with a density of 1 or more pores per an area of 50 μm x 50 μm, Appellant respectfully disagrees.

Appellant submits that Smith et al. only discloses a porous article having a porosity of 20% to 95% and comprising cell walls and struts defining pores of pore sizes in the range of 15 to 150 μm (paragraph [0023]). Thus, Smith et al. fails to disclose or suggest the fine communicating pores being open on an outer surface of the porous structure at a density of 1 or more pores per an area of 50 μm x 50 μm. Appellant further notes that Smith et al. fails to remedy the deficiencies discussed above with regard to the rejections of base claims 1 and 17 and those dependent therefrom.

Accordingly, Appellant respectfully submits that, even if combined, the combination of Smestad, Trieu et al., and Smith et al. would not result in the invention recited in claims 2 or 18. Appellant respectfully submits that claims 2 and 18 are patentable over Smestad, Trieu et al., and Smith et al. and respectfully request withdrawal of the obviousness rejection.

Appellant respectfully requests reversal of the rejection.

In conclusion, Appellant respectfully submits that each and every pending claim of the present application meets requirements for patentability, and that the present application and each pending claim are allowable over the prior art of record. Appellant respectfully requests reversal of the outstanding rejections for obviousness.

Respectfully submitted,
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## VIII. Claims Appendix

1. A bone-powder-impregnated, porous structure comprising a porous matrix made of a biocompatible material impregnated with fine bone powder obtained by pulverizing living bones and/or teeth, wherein the fine bone powder comprises sub-micron particles.

2. The bone-powder-impregnated, porous structure according to claim 1, wherein it has fine communicating pores having an average diameter of 0.005-50 μm in its entire body, said fine communicating pores being open on an outer surface of said porous structure at a density of 1 or more pores per an area of 50 μm x 50 μm.

5. The bone-powder-impregnated, porous structure according to claim 1, wherein said biocompatible material is at least one selected from the group consisting of ceramics, metals, and polymers.

6. The bone-powder-impregnated, porous structure according to claim 5, wherein said ceramics are calcium phosphate ceramics.

9. The bone-powder-impregnated, porous structure according to claim 1, wherein said fine bone powder has an average diameter of 50 μm or less.

10. The bone-powder-impregnated, porous structure according to claim 1, wherein the entire structure is porous.

14. An artificial bone comprising the bone-powder-impregnated, porous structure recited in claim 10.

17. A bone-powder-impregnated, surface-roughened structure comprising a surface-roughened matrix made of a biocompatible material, which is impregnated with fine bone powder obtained by pulverizing living bones and/or teeth, wherein the fine bone powder comprises sub-micron particles.

18. The bone-powder-impregnated, surface-roughened structure according to claim 17, wherein said surface-roughened structure has fine recesses having an average diameter of 0.005-50 μm and an average depth of 0.005-50 μm, which are open on its entire outer surface at a density of 1 or more pores per an area of 50 μm x 50 μm.

19. The bone-powder-impregnated, surface-roughened structure according to claim 17, wherein said biocompatible material is at least one selected from the group consisting of ceramics, metals, and polymers.

22. The bone-powder-impregnated, surface-roughened structure according to claim 17, wherein said fine bone powder has an average diameter of 50 μm or less.

25. An artificial bone comprising the bone-powder-impregnated, surface-roughened structure recited in claim 17.

26. An artificial dental root comprising the bone-powder-impregnated, surface-roughened structure recited in claim 17.

27. The bone-powder-impregnated, porous structure according to claim 1, wherein said fine bone powder is provided from autologous bone.

28. The bone-powder-impregnated, surface-roughened structure according to claim 17, wherein said fine bone powder is provided from autologous bone.

## IX. Evidence Appendix

None.

## X. Related Proceedings Appendix

None.